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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,675	07/06/2006	Florian Thaler	2503-1214	9608

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,675	THALER ET AL.	
	Examiner	Art Unit	
	JASON NOLAN	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/18/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicants Preliminary Amendment, filed 05/18/2006. New Claims 7-16 are pending in the instant application. Claims 1-6 are canceled.

Information Disclosure Statement

Applicants' information disclosure statement (IDS), filed on 05/18/2006 has been considered. Please refer to Applicants' copy of the 1449 submitted herein.

Claim Rejections - 35 USC §§ 101 & 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 provides for *the use of* compounds of the formula I, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 9 is rejected under 35 U.S.C. § 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper

definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. § 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 7, 8, & 10-16 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-5 of U.S. Patent No. 5,912,242. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the process of making have substantial overlap. Specifically, the instant compounds, wherein R1 is an alkyl substituted with a phenyl, is the gist of the '242 Patent. Further, there are overlapping species in the instant Claim 10 and Claim 9 of the '242 Patent. Such a subgenus is not patentably distinct and would provide unfair extended patent rights to the Applicant. A terminal disclaimer or a sufficient amendment which severs the overlap would suffice to overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7, 8, & 10-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Pevarello et al. (WO 97/05111; *see* IDS). Specifically, the instant compounds wherein R1 is an alkyl substituted with a phenyl, is the gist of WO 97/05111. Further, there are overlapping species in the instant Claim 10 and WO 97/05111; such as i.e. 3-[4-((2-fluorobenzyloxy)-benzylamino]-pyrrolidin-2-one.

Claims 7 rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki et al. (JP 01204073 A, 08/16/1989; *see* attached CAS Abstract and structure). Disclosed in the patent is compound RN 120134-94-3, which anticipates the instant formula (I) wherein X = O; R1 = Me; R4 = Me; R5 = H; and m = 3.

Claim Rejections - 35 USC § 112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-16 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while enabling for compounds (and compositions) and a method of making treating pain and other disorders such as inflammatory pain, hypertension, arrhythmias, and diabetes, is not enabled for the treatment of the generic classes of diseases such as cognitive disorders, inflammation, gastrointestinal tract disorders, and disorders of the genitor urinary tract that are encompassed within the scope of the

instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01(a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'."

In re Wands, 8 USPQ2d 1400 (1988), discusses the following factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph:

1. *The nature of the invention;*
2. *The state of the prior art;*
3. *The predictability or lack thereof in the art;*
4. *The amount of direction or guidance present;*
5. *The presence or absence of working examples;*
6. *The breadth of the claims;*
7. *The quantity of experimentation needed; and*
8. *The level of skill in the art*

each of which is discussed in turn below.

The nature of the invention

The nature of the invention of Claims 12-16 is the use of a compound according to Formula (I) for the treatment of diseases that are modulated by the calcium and/or sodium channel, for example, hypertension.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art, namely pharmacological art, involves screening *in vitro* and *in vivo* to determine if the compounds exhibit desired pharmacological activities, which are then tested for their efficacy on human beings. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The instant claimed invention is highly unpredictable as discussed below.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. *In the instant case,* the claimed invention is highly unpredictable since one skilled in the art would recognize that a group of compounds and compositions may act as calcium and/or sodium channel blockers that have involvement (either directly or peripherally within the mechanism of action) in certain diseases; but, it does not mean that the same group of compounds and compositions may treat all diseases associated with the calcium and/or sodium ion channels.

To date, there have been many reviews that establish calcium and/or sodium ion channel blockers as potential therapeutics for diseases such as pain and other disorders such as inflammatory pain, hypertension, arrhythmias, ophthalmic disorders, and diabetes. For instance, Ragsdale et al. (Brain Research Reviews 1998, 26, 16-28)

provides for sodium channels as molecular targets for antiepileptic drugs; Leong et al. (Pain Medicine 2001, 2(3), 228-229) reviews a sodium channel blocker for the treatment of ophthalmic changes; Sica, D.A. (The Journal of Clinical Hypertension 2006, 8(1), 53-56) reviews calcium channel blockers for pharmacotherapy; Sabido-David (Expert. Opinion Investig. Drugs 2004, 13(10), 1249-1261) and Priest et al. (PNAS 2007, 104(20), 8205-06) review the use of calcium channel blockers and the treatment of pain.

However, it has not been established that calcium and/or sodium ion channel blockers can be used to treat cognitive disorders such as Parkinson's disease, Alzheimer's disease, gastrointestinal tract disorders such as Crohn's disease, etc. Therefore, support from the prior art is lacking, and it is essential that the specification provide for the lack of support in order for one of skill in the art to use these compounds as pharmaceuticals as claimed.

The amount of direction or guidance present and the presence or absence of working examples

The direction or guidance present in Applicants' Specification provides evidence that establishes the compounds of the present invention as active in at least one assay selected from Examples 8-13; *see* Biological Examples on pp. 27-32. Some *in vivo* data has been provided (pain) to support the scope of the instant claims. However, there is not sufficient data present to support the broad claim for cognitive disorders, inflammation (generally), gastrointestinal tract disorders, or disorders of the genitor urinary tract.

The breadth of the claims, quantity of experimentation, and level of skill in the art

Claims 12-16 are drawn to a compound according to Formula (I) for the treatment of diseases that are modulated calcium and/or sodium channel blockers, for example, hypertension. In order to treat a disease, one would need to demonstrate what the subject population is, what the necessary dose is for efficacy and that the subject has recovered from such a disease. The potential of calcium and/or sodium channel blockers for the treatment of some diseases has been established herein; however, not for generic classes of diseases (i.e. cognitive disorders).

Because of the aforementioned reasons, a person of skill in the art could not practice the claimed invention herein, or a person of skill in the art could practice the claimed invention herein only with undue experimentation and with no assurance of success. Examiner suggests amending the scope of the claims to include only the diseases from that have been established in the prior art, as pointed out herein.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jason M. Nolan, Ph.D.** whose telephone number is **(571) 272-4356** and electronic mail is Jason.Nolan@uspto.gov. The examiner can normally be reached on Mon - Fri (9:00 - 5:30PM). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph M^{c}Kane** can be reached on **(571) 272-0699**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jason M. Nolan, Ph.D./

Examiner, Art Unit 1626

/Joseph K McKane/

Supervisory Patent Examiner, Art Unit 1626